Tues 21 st.

Title	Fifth International Workshop on Papillomavirus
Location	C.S.H. September 3 - 7, 1986
Expected Number of Participants	150 participants representing some 50 laboratories from the US and other countries.
Type of Audience	Mixture of molecular biologists, virologists, cell biologists, pathologists, otolaryngologists gynecologists and dermatologists.
Publicity Plans	Clasified ads in the following Journals: Science Cell Nature J. Investigative Dermatology International J. Gynecologic Pathologists American Society Microbiology New NIH Forgarty Center Calendar of Meetings World Meetings Information Center Calendar JAMA
Publications of Proceedings	For the workshop the submitted abstracts will be printed in an Abstract Booklet. This workshop will constitute one of Cancer Cell Series, CSH and invited papers will be published by CSH in book form.

Justification of Conference

Papillomaviruses are a group of related viruses which cause benign epithelial tumors in their human and animal hosts. It has been estimated that between 1 and 10% of the women in the United States have cervical papillomavirus infections, indicating the importance of papillomaviruses as a current health problem. There is growing evidence that some of these viruses also have the potential to cause malignant tumors. Papillomaviruses are most probbly a major factor in the etiology of human cervical and penile carcinomas, and may play a significant role in some other human and animal carcinomas. The isolation of new papillomaviruses, the interaction of these viruses with their target cells, the epidemiology of human papillomavirus induced diseases, the regulation and transcription of viral genomes, and the use of the cloned viruses as vectors in eubaryotic cells are under intensive study in many laboratories. This workshop addresses the needs of this heterogenous group of scientists and clinicians for information on the most recent advances in the field of papillomaviruses.

At the present time in the field of papillomavirus research, there is general consensus that five key areas must be developed: 1) an understanding of the molecular organization and regulated expression of papillomavirus genomes; 2) a model for the study of viral cell interactions; 3) an effective method for screening clinical material to identify the specific papillomavirus type involved; 4) a clear description of the clinical course of special papillomavirus infections; and 5) an evaluation of new modalities of therapy. These five areas are inter-related, and the disciplines involved are diverse. Therefore, exchanges of ideas and techniques

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are needed, and continual dialogue among basic and clinical investigators is vital.

The widespread interest in papillomavirus research is rather recent and is marked by a rapid expansion of new information and new techniques. The newness of the field and the rapidity of research has meant that a significant proportion of the information has not yet been published. Therefore, for new investigators, meetings are an essential mechanism to become current in the field. We plan on holding two short courses in terminology and basic concepts for newcomers. The lack of standardization of new techniques has also been problematic, and we plan to hold mini-workshops to discuss this problem.

There is also considerable commercial interest in developing effective therapeutic measures for papillomavirus related diseases. In the past this workshop has provided and will continue to provide fruitful interactions.

History

Although papillomaviruses were the first tumor viruses to be discovered,it was not until the 1970's that techniques become available for their identification and study. As new information was received about the widespread nature of their agents, concern grew for the possible health hazards they posed. The first international workshop on papillomaviruses was held at CSH in September 1982 to bring together the assorted scientists and clinicians who share a common interest in these viruses. Since that time, workshops have been held annually in the late summer in Sweden (1983), Japan (1984) and Finland (1985). A workshop format has been adopted because of the newness of the subject area, the rapid pace of research, and the necessity for interactions between clinical and basic biological investigators. These meetings have attracted about 125 participants each year, of whom about 15 are "new faces". An additional meeting, organized by the UCLA Continuing Education Program, was held in April 1985 in Steamboat Springs, and a Banbury conference with limited attendance on viruses and cancer was held immediately after that meeting. Neither of these were within the framework of the regularly scheduled International Workshop. The fact that they were held attests to the intensive interest in this field.

Format

Dedication

This meeting will be dedicated to Dr. Richard E. Shope and Dr. Yohei Ito. A lecture by Dr. Carl Olson (University of Wisconsin) will begin the program and will recount the pioneering work of these two individuals in the field of papillomavirus research.

Plenary Session

Plenary sessions will be held in the morning ($3\frac{1}{2}$ hrs) and in the evening ($1\frac{1}{2}$ hrs). Each session will cover a major area of interest. The invited speakers will be asked to review the subject matter in their particular area and to summarize as best as possible the most up to date results. Talks will be 40 mins. in length including time for discussion. These sessions are intended to serve the needs of both established and new investigators for a comprehensive coverage of the subject matter.

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Posters

To ensure that all attendees will be able to participate and to allow invited speakers to present their recent data in detail, all participants will be invited to prepare posters describing their recent research findings. The poster sessions will be held following the evening plenary session. Each poster session will be related in topic to the plenary sessions of that day.

Mini-Workshops on Methodologies

In past meetings, frequent questions arose dealing with differences in methodologies. The questions centered around screening for PV types, in situ hybridization and epithelial cell culture. Informal one hour mini-workshops are planned on each of these topics to permit new and established investigators to discuss these issues. A workshop chairperson will be asked to introduce the topic and lead the discussion. These workshops will be held simultaneously during one afternoon.

Mini-Courses

Because papillomavirus research spans diverse areas from the molecular to the clinical, investigators (established and new) have often been frustrated by the "foreign" terms used by the other discipline. Two one hour mini-courses will be offered on Molecular Biology for clinicians as well as Clinical Terms for the molecular biologist.

Cancer Cell Book - CSH Publication

All invited speakers will be asked to submit manuscripts at or shortly following the meeting. All other participants whose abstracts have been accepted will be invited to submit manuscripts at the time of the meeting. All manuscripts will be due by October 15.

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Outline of Agenda

1. Dedication "Richard Shope and Yohei Ito: The Beginnings of Papillomavirus Research"
2. Animal Viruses and Animal Disease
3. Human Disease and Implications of Viral Heterogeneity
4. Papillomavirus Expression, Replication, Transcription and Protein Synthesis
5. Genomic Organization and Vectors
6. Transformation and Oncogenes
7. Immunologies and Therapies
8. Workshops on Methodologies:
   a. Typing and Classification
   b. In Situ Hybridization
   c. Epithelial Cell Cultures
9. Mini-Courses:
   a. Molecular Biology for the Clinician
   b. Clinical Terms for the Molecular Biologist

Sessions

1, 2. Animal Viruses and Animal Diseases

Animal papillomaviruses have historically been an important model for human diseases and an important problem in animal husbandry. The workshop will be dedicated to Drs. Richard Shope and Yohei Ito, whose pioneering efforts in animal PV's led to the establishment of the field of papillomavirus research. A commemorative lecture honoring their contribution will be held the first evening followed by research papers. Animal models have been very useful in defining host and environmental factors responsible for the conversion of a benign papilloma to a malignant carcinoma. The recent development of vaccines for BPV infection of cattle will be discussed. In addition to their possible commercial benefits, they may provide useful information on the possibility of a similar therapeutic approach in humans.

3. Human Diseases

It is now clear that human papillomavirus (HPV) infections play a role in human diseases. A large number of viral subtypes (more than 33 to date) have been identified, and some have been associated with the progression of papillomas to carcinomas. zur Hausen and his group have isolated and cloned papillomaviruses from cervical carcinomas, while J. Orth and S. Jablonska have done similar studies on cutaneous carcinomas in patients with epidermodysplasia verruciformis. K. Syrjanen is conducting a longitudinal prospective study to determine risk factors for specific types of HPV infection and progression to malignancy in cervical dysplasias. Oral and laryngeal HPV infections produce benign lesions which also have potential for malignant conversion. This session will focus on the potential of specific HPV types to induce characteristic lesions, the question of malignant conversion, and possible environmental cofactors.

4a. Viral Replication

Two features of papillomavirus replication are unique. First is the fact that in benign and in a number of malignant tumors, PV DNA is present in episomal

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form. Second is the fact that vegetative viral replication in benign lesions is confined to differentiating keratinocytes of the lesion. P. Howley, M. Botchan and others have defined regions of the BPV genome required for stable plasmid maintenance and for maintaining high copy numbers. The interaction of various mutant PV containing plasmids is currently under intensive investigation and may be helpful in defining possible control mechanisms for PV DNA replication.

To date, no culture system capable of supporting productive PV replication has been found. This points out the complex interaction between the virus and its host cell, the keratinocyte. In this session, in addition to discussing the mechanism of plasmid maintenance, we will examine the expression of PVs in cultured epithelial keratinocytes.

4b. Transcription and Proteins

Considerable advances have been made in the past few years in defining the RNA transcripts produced by PV genomes in cultured cells and in papillomatous lesions. Similarities in splicing patterns have emerged and helped us to understand some of the biological features of papillomaviruses. A long sought after goal has been the identification of viral specific proteins that are involved in transformation and cytopathic effects. Recently, monoclonal antibodies have been generated against peptides produced from specific cloned fragments of PV genomes. In several instances, low molecular weight viral proteins (17KD) have been found originating from the EH open reading frame. We anticipate that by the time of the CSH meeting, the properties of these proteins will have been partially established and new viral specific proteins identified.

5. Genome Organization and Vectors

This session covers the structure of HPV DNA molecules, the commonalities and divergences of the different papillomaviruses and the way this organization affects the biological activity of the virus. One key aspect of PV function is its ability to replicate and exist as an episome (see Section 4). This has been used by a number of investigators to construct eukaryotic vectors which do not integrate into the host genome. The applications of this techinque and the information derived from it regarding papillomavirus genomic structure and function will be discussed.

6. Transformation and Oncogenes

This session is devoted to two separate but related topics. Recent advances in PV studies, primarily in cultured cells infected with bovine papillomaviruses, have discovered two regions of the virus which effect transformation in vitro. Detection of RNA transcripts from one of these regions (E6-E7) in tumors and in permanent cell lines derived from carcinomas suggests that this region may be functional in the maintenance of transformation in vivo and in vitro. The role of cellular oncogenes and any possible relationship between putative viral transforming proteins and cellular oncogenes in HPV transformation is not known. We do know that levels of at least two cellular oncoge products, myc and ras, are altered in certain tumors containing HPV DNA and RNA transcripts. This session will address the most recent advances in both the areas of HPV transformation and role of oncogenes in HPV induced transformation, and will serve as a forum to initiate new studies on these two types of transforming genes and their interactions.

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7. Immunology and Therapy

Recent studies with interferon therapy, first initiated by H. Strander with laryngeal papillomatosis and now in large clinical trials with both laryngeal and genital HPV diseases, suggests that this immunoregulator might be a successful agent for the control or possible cure of severe HPV infections. The immunobiology of papillomaviruses is, at present, poorly understood. Some information has been derived from studies with EV patients (see section 3) and observations that immunosuppressed persons are at high risk for cutaneous HPV lesions. F. Breitburd, K. Syrjanen and others have described specific lymphocytic infiltrates into papillomas, but the mechanism and role of immunoregulation in HPV infections has not been defined.

This session will introduce to the participants the current status of our understanding of the immunobiology of epithelial tissues and the possible role of the immune system in HPV induced disease. The role of interferon as well as other therapies under investigation will also be discussed.

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